UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,157	07/27/2007	Akihiko Kameyama	062989	7036

38834   7590   05/06/2009
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EXAMINER
XU, XIAOYUN

ART UNIT	PAPER NUMBER
1797	

MAIL DATE	DELIVERY MODE
05/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2009*.

2a)☒ This action is **FINAL**.   2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

    4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

    a)☐ All   b)☐ Some * c)☐ None of:

      1.☐ Certified copies of the priority documents have been received.

      2.☐ Certified copies of the priority documents have been received in Application No. _____.

      3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

    * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO/SB/08)
    Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413)
    Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

DETAILED ACTION

1.   The amendment filed 03/23/2009 has been entered and fully considered. Claims 1-13 are pending, of which Claims 1 and 13 are amended.

Response to Amendment

2.   In response to amendment, the examiner withdraws 112, second paragraph, rejection and maintains rejection over the prior art established in the previous Office action.

Claim Rejections - 35 USC § 103

3.   The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4.   **Claims 1-7, 10 and 11** are rejected under 35 U.S.C. 103(a) as being unpatentable over Takegawa et al. (Rapid Communication in Mass Spectrometry, 2004, IDS) (Takegawa).

In regard to Claims 1 and 3, Takegawa teaches a method of identifying an analysis-objective sugar chain structure using a mass spectrometry by comparing a measured MS3 fragment pattern with a reference MS3 fragment pattern stored in a database, where the measured MS3 fragment pattern is a fragmentation pattern of MS2 fragment ion included in a measured MS2 fragment pattern obtained by subjecting the sugar chain to a fragmentation mass spectrometry (see abstract).

Takegawa teaches selecting MS2 fragment ions for MS3 fragmentation (see page 388, right col. 2nd paragraph, Figure 5). Takegawa also teaches that when the mutual similarity (correlation coefficient) among the MS2 fragment patterns are small, the isomers of the sugar can be differentiated by using the fragment ion intensities of MS2 spectra (see page 387, right col. 1st paragraph, and page 388, right col. 1st paragraph). Takegawa does not specifically teach selecting MS3 precursor based on least similarity (correlation coefficient) among MS3 fragment patterns. However, Takegawa teaches the idea that when precursor has small similarity (correlation coefficient) among the fragment patterns, the isomers of the sugar can be differentiated

by the fragmentation pattern (see page 388, right col. 1st paragraph). Takegawa applied this idea on determining whether the MS2 fragment patterns will differentiate the isoforms. It would have been obvious for one of ordinary skill in the art to apply the same idea on selecting the precursor of MS3 fragment patterns, because this is will facilitate the quick identification of the isoforms. Takegawa also teaches developing a reliable MSn database designed for oligosaccharide structural assignment (see page 390, left col.).

In regard to Claims 2 and 4, Takegawa does not specifically teach using MS4 or MSn fragment patterns to identify a sugar chain. However, Takegawa teaches developing a reliable MSn database designed for oligosaccharide structural assignment (see page 390, left col.). From MS3 to MS4 or MSn and selecting the precursor for MS4 or MSn is a natural extension of the technology, because it simply repeats the same process of from MS2 to MS3 by choosing a MS3 fragment as the precursor of MS4 and measure the fragment pattern of MS4. It would have been obvious for one of ordinary skill in the art to use the idea of using the fragment patterns of least mutual similarity (correlation coefficient) to differentiate the isoforms as taught by Takegawa in Takegawa's method to further extend the fragment pattern from MS3 to MS4 or MSn with reasonable expectation that this would provide more information for recognizing the isoforms of the sugar chain.

In regard to Claim 5, storing reference MSn+1 fragment patterns in the database by associating with a mass to charge ratio of the precursor ion is known in the art and also taught by Takegawa (see page 390).

In regard to Claim 6, Takegawa teaches selecting MSn with strong peak (m/z 790) as the precursor of MSn+1 fragment pattern (see page 387).

In regard to Claim 7, Takegawa teaches that a theoretical composition of sugar chain can be calculated from a measured MSn fragment pattern and MSn+1 fragment patterns stored in the database can be used to further differentiate the isoforms (see page 390). Based on the teaching of Takegawa, it would have been obvious to ordinary skill in the art that the patterns to be compared are restricted in advance.

In regard to Claim 10, calculating Euclidean distance between two vectors as the measure of difference of the two vectors is known in the art. Takegawa teaches calculating correlation coefficient of the two fragment patterns in a similar way (see page 387, right col. 1st paragraph). At the time of the invention, it would have been obvious to one of ordinary skill the art to calculate the dissimilarity of the fragment patterns from the Euclidean distance of the vectors.

In regard to Claim 11, reversing the order of fragment patterns and performing the same Euclidean distance calculation is still a routine calculation of mutual dissimilarity.

5.   **Claims 8, 9, 12 and 13** are rejected under 35 U.S.C. 103(a) as being unpatentable over Takegawa in view of Armentrout (Topics of Current Chemistry, 2003).

In regard to Claims 8 and 9, Takegawa does not specifically teach setting specific fragmentation energy for the fragmentation mass spectroscopy. The fragmentation energy of the fragmentation mass spectroscopy is the energy used for breaking the molecule into fragment. It should be higher or equal to threshold collision-induced dissociation energy which is the minimum energy required to break the molecule. Armentrout teaches how to determine the threshold collision-induced dissociation energy (see abstract). At the time of the invention it would have been obvious to one of ordinary skill in the art to store threshold collision-induced dissociation energy of the precursor in the database and set the fragmentation energy higher than the threshold collision-induced dissociation energy of the precursor in the database so that the precursor will be fragmented, because having a higher energy of fragmentation is a necessary requirements for fragmenting molecules in mass spectrometry.

In regard to Claim 12, Takegawa teaches a mass spectrometer for analyzing a sugar chain, which comprises:

a mass spectroscopy part equipped with a means for holding and fragmenting an ion (see page 386),

a database part in which MSn fragment patterns of known sugar chains are stored (see page 390), and

a data processing part for controlling the mass spectrometer (see abstract)

In regard to Claim 13, a computer readable medium encoded with a program causing a computer to carry out the method is inherent to Takegawa's teaching (see abstract).

Response to Arguments

6.   Applicant's arguments filed 03/23/2009 have been fully considered but they are not persuasive.

Applicant argue that Takegawa does not disclose, teach, suggest or provide any reason to use a method of choosing the most suitable MS2 fragment ion base on "mutual similarity index" calculated among reference fragment patterns for ions having the same mass to charge ratio as one of the MS2 fragment ions. Takegawa teaches "correlation coefficient" (see page 388, right col. 1st paragraph) which is the same idea of "mutual similarity index". Low "correlation coefficient" means low "mutual similarity index". Takegawa teaches that when the calculation of correlation coefficient is low (0.624, 0.000, and 0.238), the fragment pattern can be differentiated (see page 388, right col. 1st paragraph). Therefore, it would have been obvious to one of ordinary skill in the art to select precursor of MSn, wherein, MSn of isoforms has low "correlation coefficient" among them, or in other word, MSn of isoforms has low "mutual similarity index". Takegawa further teaches that matching MSn spectra based on correlation coefficients is a useful approach applicable to the structural assignment (see page 390, right col. 2nd paragraph).

Conclusion

7.   **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT XU whose telephone number is (571)270-5560. The examiner can normally be reached on Mon-Thur 7:30am-5:00pm, Fri 7:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

5/4/2009   /Yelena G. Gakh/
                                                           Primary Examiner, Art Unit 1797

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